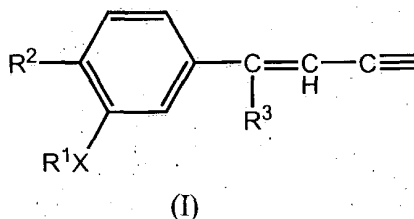


1 What is claimed is:

2  
3 1. A substantially pure (E)-compound, a substantially pure (Z)-compound, or a  
4 mixture of (E)- and (Z)-compounds having the formula (I):



5  
6  
7  
8 wherein:

9  
10 (a) X is -O- or -(C<sub>n</sub>H<sub>2n</sub>)- in which *n* has a value of 0, 1, 2, or 3, and R<sup>1</sup> is selected  
11 from the group consisting of any alkyl of up to 10 carbon atoms, any  
12 monocycloalkyl of up to 10 carbon atoms, any polycycloalkyl of up to 10 carbon  
13 atoms, and any benzocyclic alkyl of up to 10 carbon atoms, or

14 (b) X is -CH=, and R<sup>1</sup> is any alkylidene of up to 10 carbon atoms or any  
15 monocycloalkylidene of up to 10 carbon atoms;

16  
17 R<sup>2</sup> is hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy,  
18 acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, lower alkyl, lower alkoxy, or  
19 halo; and

20  
21 R<sup>3</sup> is (i) phenyl or naphthyl, each unsubstituted or substituted with 1 or more substituents  
22 each selected independently from the group consisting of a nitro, a cyano, a halo, a  
23 trifluoromethyl, a carbethoxy, a carbomethoxy, a carbopropoxy, an acetyl, a  
24 carbamoyl, a carbamoyl substituted with an alkyl of 1 to 3 carbon atoms, an acetoxo,  
25 a carboxy, a hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon  
26 atoms, an alkyl or cycloalkyl of 1 to 10 carbon atoms, and an alkoxy or cycloalkoxy  
27 of 1 to 10 carbon atoms; (ii) phenyl substituted with 1 or more substituents each  
28 selected independently from the group consisting of an alkylidenemethyl of up to 10

1 carbon atoms, a cycloalkylidenemethyl of up to 10 carbon atoms, a phenyl, and a  
2 methylenedioxy; (iii) cycloalkyl of 4 to 10 carbon atoms, unsubstituted or  
3 substituted with one or more substituents each selected independently from the  
4 group consisting of a nitro, a cyano, a halo, a trifluoromethyl, a carbethoxy, a  
5 carbomethoxy, a carbopropoxy, an acetyl, a carbamoyl, an acetoxo, a carboxy, a  
6 hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon atoms, an  
7 alkyl of 1 to 10 carbon atoms, an alkoxy of 1 to 10 carbon atoms, and a phenyl; or  
8 (iv) pyridine, substituted pyridine, pyrrolidine, imidazole, or thiophene.  
9

10 2. The compound or mixture of claim 1, wherein:  
11

12 X is -O- or  $-(C_nH_{2n})-$  in which  $n$  has a value of 0, 1, 2, or 3;  
13

14  $R^1$  is any alkyl of up to 10 carbon atoms, any monocycloalkyl of up to 10 carbon atoms, any  
15 polycycloalkyl of up to 10 carbon atoms, or any benzocyclic alkyl of up to 10 carbon  
16 atoms;  
17

18  $R^2$  is hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy,  
19 acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, lower alkyl, lower alkoxy, or  
20 halo; and  
21

22  $R^3$  is (i) phenyl or naphthyl, each unsubstituted or substituted with 1 or more substituents  
23 each selected independently from the group consisting of a nitro, a cyano, a halo, a  
24 trifluoromethyl, a carbethoxy, a carbomethoxy, a carbopropoxy, an acetyl, a  
25 carbamoyl, a carbamoyl substituted with an alkyl of 1 to 3 carbon atoms, an acetoxo,  
26 a carboxy, a hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon  
27 atoms, an alkyl or cycloalkyl of 1 to 10 carbon atoms, and an alkoxy or cycloalkoxy  
28 of 1 to 10 carbon atoms; (ii) phenyl substituted with 1 or more substituents each  
29 selected independently from the group consisting of an alkylidenemethyl of up to 10  
30 carbon atoms, a cycloalkylidenemethyl of up to 10 carbon atoms, a phenyl, and a  
31 methylenedioxy; (iii) cycloalkyl of 4 to 10 carbon atoms, unsubstituted or

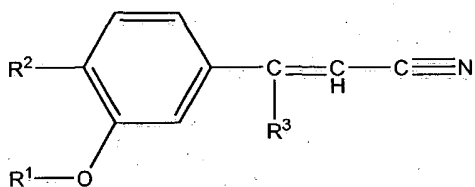
1 substituted with one or more substituents each selected independently from the  
2 group consisting of a nitro, a cyano, a halo, a trifluoromethyl, a carbethoxy, a  
3 carbomethoxy, a carbopropoxy, an acetyl, a carbamoyl, an acetoxy, a carboxy, a  
4 hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon atoms, an  
5 alkyl of 1 to 10 carbon atoms, an alkoxy of 1 to 10 carbon atoms, and a phenyl; or  
6 (iv) pyridine, substituted pyridine, pyrrolidine, imidazole, or thiophene.

7  
8 3. The compound or mixture of claim 2, wherein:

9  $R^2$  is hydrogen, nitro, cyano, trifluoromethyl, amino, lower alkyl, lower alkoxy, or halo; and

10  
11  $R^3$  is (i) phenyl or naphthyl, each unsubstituted or substituted with 1 or more substituents  
12 each selected independently from the group consisting of a nitro, a cyano, a halo, a  
13 trifluoromethyl, a carbethoxy, a carbomethoxy, a carbopropoxy, an acetyl, a  
14 carbamoyl, a carbamoyl substituted with an alkyl of 1 to 3 carbon atoms, an acetoxy,  
15 a carboxy, a hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon  
16 atoms, an alkyl or cycloalkyl of 1 to 10 carbon atoms, and an alkoxy or cycloalkoxy  
17 of 1 to 10 carbon atoms; (ii) phenyl substituted with 1 or more substituents each  
18 selected independently from the group consisting of an alkylidenemethyl of up to 10  
19 carbon atoms, a cycloalkylidenemethyl of up to 10 carbon atoms, a phenyl, and a  
20 methylenedioxy; (iii) cycloalkyl of 4 to 10 carbon atoms, unsubstituted or  
21 substituted with one or more substituents each selected independently from the  
22 group consisting of a nitro, a cyano, a halo, a trifluoromethyl, a carbethoxy, a  
23 carbomethoxy, a carbopropoxy, an acetyl, a carbamoyl, an acetoxy, a carboxy, a  
24 hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon atoms, an  
25 alkyl of 1 to 10 carbon atoms, an alkoxy of 1 to 10 carbon atoms, and a phenyl; or  
26 (iv) pyridine, substituted pyridine, pyrrolidine, imidazole, or thiophene.

27  
28 4. The compound or mixture of claim 1, wherein the compound formula (I) is:  
29



R<sup>1</sup> is alkyl of up to 10 carbon atoms;

R<sup>2</sup> is hydrogen, trifluoromethyl, lower alkyl, or lower alkoxy; and

R<sup>3</sup> is (i) phenyl or naphthyl, each unsubstituted or substituted with 1 or more substituents each selected independently from the group consisting of a nitro, a cyano, a halo, a trifluoromethyl, a carbethoxy, a carbomethoxy, a carbopropoxy, an acetyl, a carbamoyl, a carbamoyl substituted with an alkyl of 1 to 3 carbon atoms, an acetoxyl, a carboxy, a hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon atoms, an alkyl or cycloalkyl of 1 to 10 carbon atoms, and an alkoxy or cycloalkoxy of 1 to 10 carbon atoms; (ii) phenyl substituted with 1 or more substituents each selected independently from the group consisting of an alkylidenemethyl of up to 10 carbon atoms, a cycloalkylidenemethyl of up to 10 carbon atoms, a phenyl, and a methylenedioxy; (iii) cycloalkyl of 4 to 10 carbon atoms, unsubstituted or substituted with one or more substituents each selected independently from the group consisting of a nitro, a cyano, a halo, a trifluoromethyl, a carbethoxy, a carbomethoxy, a carbopropoxy, an acetyl, a carbamoyl, an acetoxyl, a carboxy, a hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon atoms, an alkyl of 1 to 10 carbon atoms, an alkoxy of 1 to 10 carbon atoms, and a phenyl; or (iv) pyridine, substituted pyridine, pyrrolidine, imidazole, or thiophene.

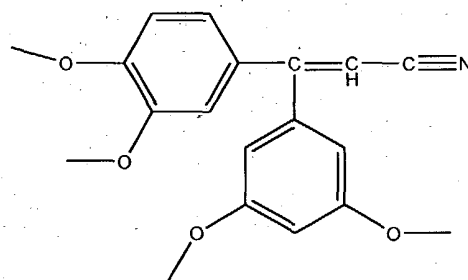
5. The compound of claim 4, wherein:

R<sup>1</sup> is methyl or ethyl;

1  $R^2$  is methoxy or ethoxy;

2  
3  $R^3$  is (i) phenyl or naphthyl, each unsubstituted or substituted with 1 or more substituents  
4 each selected independently from the group consisting of a nitro, a cyano, a halo, a  
5 trifluoromethyl, a carbethoxy, a carbomethoxy, a carbopropoxy, an acetyl, a  
6 carbamoyl, a carbamoyl substituted with an alkyl of 1 to 3 carbon atoms, an acetoxy,  
7 a carboxy, a hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon  
8 atoms, an alkyl or cycloalkyl of 1 to 10 carbon atoms, and an alkoxy or cycloalkoxy  
9 of 1 to 10 carbon atoms; (ii) phenyl substituted with 1 or more substituents each  
10 selected independently from the group consisting of an alkylidenemethyl of up to 10  
11 carbon atoms, a cycloalkylidenemethyl of up to 10 carbon atoms, a phenyl, and a  
12 methylenedioxy; (iii) cycloalkyl of 4 to 10 carbon atoms, unsubstituted or  
13 substituted with one or more substituents each selected independently from the  
14 group consisting of a nitro, a cyano, a halo, a trifluoromethyl, a carbethoxy, a  
15 carbomethoxy, a carbopropoxy, an acetyl, a carbamoyl, an acetoxy, a carboxy, a  
16 hydroxy, an amino, an amino substituted with an alkyl of 1 to 5 carbon atoms, an  
17 alkyl of 1 to 10 carbon atoms, an alkoxy of 1 to 10 carbon atoms, and a phenyl; or  
18 (iv) pyridine, substituted pyridine, pyrrolidine, imidazole, or thiophene.

19  
20 6. A substantially pure (E)-compound, a substantially pure (Z)-compound, or a  
21 mixture of (E)- and (Z)-compounds having the formula (II):



(II).

22  
23  
24  
25  
26 7. The compound of claim 1 wherein the compound is selected from:

- 1 3,3-*bis*-(3,4-dimethoxyphenyl)acrylonitrile;
- 2
- 3 3,3-*bis*-(3-ethoxy-4-methoxyphenyl)acrylonitrile;
- 4
- 5 3-(3-propoxy-4-methoxyphenyl)-3-phenylacrylonitrile;
- 6
- 7 3-(3-ethoxy-4-methoxyphenyl)-3-phenylacrylonitrile;
- 8
- 9 3,3-*bis*-(3-cyclopentoxy-4-methoxyphenyl)acrylonitrile;
- 10
- 11 3-(3-cyclopentoxy-4-methoxyphenyl)-3-phenylacrylonitrile;
- 12
- 13 3-(3,4-dimethoxyphenyl)-3-phenylacrylonitrile;
- 14
- 15 3-(3,4-Dimethoxyphenyl)-3-(3',5'-dimethoxyphenyl)-
- 16 acrylonitrile;
- 17
- 18 3-(3, 4-Dimethoxyphenyl)-3-(3-ethoxy-4-methoxyphenyl)acrylonitrile;
- 19
- 20 3-(3,4-Dimethoxyphenyl)-3-(3'-nitrophenyl)acrylonitrile;
- 21
- 22 3-(3'-Aminophenyl)-3-(3,4-dimethoxyphenyl)acrylonitrile;
- 23
- 24 3-(3,4-Dimethoxyphenyl)-3-(4-nitrophenyl)acrylonitrile;
- 25
- 26 3-(4-Aminophenyl)-3-(3,4-dimethoxyphenyl)acrylonitril;
- 27
- 28 3-(4-Aminophenyl)-3-(3,4-dimethoxyphenyl)acrylonitrile;
- 29
- 30 3-(4-Biphenyl)-3-(3,4-dimethoxyphenyl)acrylonitrile;
- 31

1 3-(3,4-Dimethoxyphenyl)-3-(4'-fluorophenyl)acrylonitrile;  
2  
3 3-(3,4-Dimethoxyphenyl)-3-naphth-2-ylacrylonitrile;  
4  
5 3-(3,4-Dimethoxyphenyl)-3-(3,4-methylenedioxyphenyl)acrylonitrile;  
6  
7 3-(3,4-Dimethoxyphenyl)-3-pyridin-4-ylacrylonitrile;  
8  
9 3-(3,4-Dimethoxyphenyl)-3-pyridin-2-ylacrylonitrile;  
10  
11 3-(3,4-Dimethoxyphenyl)-3-(2-furyl)acrylonitrile;  
12  
13 3-(3,4-Diethylphenyl)-3-phenylacrylonitrile;  
14  
15 3-(3,4-Diethylphenyl)-3-(3,4-dimethoxyphenyl)acrylonitrile;  
16  
17 3-(3,4-Dimethoxyphenyl)-3-(naphth-1-yl)acrylonitrile; and  
18  
19 3-(3,4-Dimethoxyphenyl)-3-(2,5-dichlorophenyl)acrylonitrile.  
20

21 8. A method which comprises administering to a mammal an amount of a  
22 compound or mixture according to claim 1, said amount being effective to mediate the  
23 action of a phosphodiesterase.  
24

25 9. The method of claim 8, wherein said phosphodiesterase is a  
26 phosphodiesterase selected from the group consisting of PDE III and PDE IV.  
27

28 10. A method which comprises administering to a mammal an amount of a  
29 compound or a mixture according to claim 1, said amount being effective to mediate the  
30 formation or action of TNF $\alpha$ .  
31

1           11.     A method which comprises administering to a mammal an amount of a  
2 compound or a mixture according to claim 1, said amount being effective to mediate the  
3 formation or action of NFκB.

4

5           12.     A pharmaceutical composition comprising a compound or mixture according  
6 to claim 1.

7

8           13.     A method which comprises administering to a mammal an amount of a  
9 compound or mixture according to claim 1, said amount being effective for treating one  
10 or more conditions selected from the group consisting of septic shock, sepsis, endotoxic  
11 shock, hemodynamic shock and sepsis syndrome, post ischemic reperfusion injury,  
12 malaria, mycobacterial infection, meningitis, psoriasis, congestive heart failure, fibrotic  
13 disease, cachexia, graft rejection, cancer, autoimmune disease, opportunistic infections in  
14 AIDS, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, other arthritic  
15 conditions, Crohn's disease, ulcerative colitis, multiple sclerosis, systemic lupus  
16 erythematosus, ENL in leprosy, radiation damage, asthma, and hyperoxic alveolar injury.

17           14.     A method which comprises administering to a mammal an amount of a  
18 compound or mixture according to claim 1, said amount being effective for treating  
19 cancer.

20           15.     A method which comprises administering to a mammal an amount of a  
21 compound or mixture according to claim 1 in combination with a second pharmaceutical  
22 agent, said amount being effective for treating cancer.

23

24           16.     A compound of claim 1 that is an (E)-compound.

25

26           17.     A compound of claim 1 that is a (Z)-compound.

27

28           18.     A mixture of claim 1 comprising both (E)- and (Z)- compounds.



1           19.     A method which comprises administering to a mammal an amount of a  
2 compound or mixture according to claim 4, said amount being effective to mediate the  
3 action of a phosphodiesterase.

4  
5           20.     The method of claim 19, wherein said phosphodiesterase is a  
6 phosphodiesterase selected from the group consisting of PDE III and PDE IV.

7  
8           21.     A method which comprises administering to a mammal an amount of a  
9 compound or a mixture according to claim 4, said amount being effective to mediate the  
10 formation or action of TNF $\alpha$ .

11  
12           22.     A method which comprises administering to a mammal an amount of a  
13 compound or a mixture according to claim 4, said amount being effective to mediate the  
14 formation or action of NF $\kappa$ B.

15  
16           23.     A pharmaceutical composition comprising a compound or mixture according  
17 to claim 4.

18  
19           24.     A method which comprises administering to a mammal an amount of a  
20 compound or mixture according to claim 4, said amount being effective for treating one  
21 or more conditions selected from the group consisting of septic shock, sepsis, endotoxic  
22 shock, hemodynamic shock and sepsis syndrome, post ischemic reperfusion injury,  
23 malaria, mycobacterial infection, meningitis, psoriasis, congestive heart failure, fibrotic  
24 disease, cachexia, graft rejection, cancer, autoimmune disease, opportunistic infections in  
25 AIDS, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, other arthritic  
26 conditions, Crohn's disease, ulcerative colitis, multiple sclerosis, systemic lupus  
27 erythematosus, ENL in leprosy, radiation damage, asthma, and hyperoxic alveolar injury.

1           25.    A method which comprises administering to a mammal an amount of a  
2 compound or mixture according to claim 4, said amount being effective for treating  
3 cancer.

4           26.    A method which comprises administering to a mammal an effective  
5 amount of a compound or mixture according to claim 4 in combination with a second  
6 pharmaceutical agent, said amount being effective for treating cancer.

7  
8           27.    A compound of claim 4 that is an (E)-compound.

9  
10          28.    A compound of claim 4 that is a (Z)-compound.

11  
12          29.    A mixture of claim 4 comprising both (E)- and (Z)- compounds.

13  
14          30.    A method which comprises administering to a mammal an amount of a  
15 compound or mixture according to claim 6, said amount being effective to mediate the  
16 action of a phosphodiesterase.

17  
18          31.    The method of claim 30, wherein said phosphodiesterase is a  
19 phosphodiesterase selected from the group consisting of PDE III and PDE IV.

20  
21          32.    A method which comprises administering to a mammal an amount of a  
22 compound or a mixture according to claim 6, said amount being effective to mediate the  
23 formation or action of TNF $\alpha$ .

24  
25          33.    A method which comprises administering to a mammal an amount of a  
26 compound or a mixture according to claim 6, said amount being effective to mediate the  
27 formation or action of NF $\kappa$ B.

- 1  
2 34. A pharmaceutical composition comprising a compound or mixture according  
3 to claim 6.  
4
- 5 35. A method which comprises administering to a mammal an amount of a  
6 compound or mixture according to claim 6, said amount being effective for treating one  
7 or more conditions selected from the group consisting of septic shock, sepsis, endotoxic  
8 shock, hemodynamic shock and sepsis syndrome, post ischemic reperfusion injury,  
9 malaria, mycobacterial infection, meningitis, psoriasis, congestive heart failure, fibrotic  
10 disease, cachexia, graft rejection, cancer, autoimmune disease, opportunistic infections in  
11 AIDS, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, other arthritic  
12 conditions, Crohn's disease, ulcerative colitis, multiple sclerosis, systemic lupus  
13 erythematosus, ENL in leprosy, radiation damage, asthma, and hyperoxic alveolar injury.
- 14 36. A method which comprises administering to a mammal an amount of a  
15 compound or mixture according to claim 6, said amount being effective for treating  
16 cancer.
- 17 37. A method which comprises administering to a mammal an effective  
18 amount of a compound or mixture according to claim 6 in combination with a second  
19 pharmaceutical agent, said amount being effective for treating cancer.  
20
- 21 38. A compound of claim 6 that is an (E)-compound.  
22
- 23 39. A compound of claim 6 that is a (Z)-compound.  
24
- 25 40. A mixture of claim 6 comprising both (E)- and (Z)- compounds.